UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,460	02/15/2002	Bettina Moeckel	218472US0X	7547

22850 7590 09/05/2003

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/075,460	Applicant(s) MOECKEL ET AL.	
	Examiner Richard G Hutson	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *12-23 and 25-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-11,24 and 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-40 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-11, 24, and 31-40, in Paper No. 6 is acknowledged. Applicants traversal is on the basis that the Office has not adequately established that Groups I, II and III are independent and distinct from one another and that no undue burden would be imposed on the Examiner in conducting an Examination of all three groups together, because of the similar subject matter encompassed by each group. Applicants traversal is not found persuasive because as previously stated, the inventions of group I and the inventions of groups II and III are each related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polynucleotide of Group I can be used in a materially different process such as one in which the polynucleotide is used to express the encoded protein for the production of antibodies. This process is different from each of the processes of groups II and II.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature

and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

While applicants submit how the subject matter of the different groups are related, it remains that the searches required for each of the above distinct groups are not coextensive, and thus restriction for examination purposes as indicated is proper.

Applicants comments with regard to the rejoinder of the nonelected groups are acknowledged, however these will be dealt with upon the indication of allowability of the elected claims as per MPEP 821.04.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-23 and 25-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

Priority

Applicants claim of priority to German Application No. 10107230.5, filed February 16, 2001 and German Application No. 10162386.0, filed December 13, 2001, is acknowledged. It is further noted that a certified copy of these priority document are present in the application file.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other

information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 4, filed 12/56/2002 and Paper No. 7, filed May 27/2003, are acknowledged. Those references considered have been initialed, while those pending applications identified by applicants in Paper No. 7 are acknowledged.

Claim Objections

Claims 6 and 7 are objected to because of the following informalities:

Claim 6 (claim 7 dependent from) is drawn to a DNA which optionally comprises a number of different structural limitations. These different limitations are each designated by "(i), (ii), (iii) or (iv)". Claim 1 also lists a number of different structural limitations, however claim 1 designates these by "a), b), c), or d)". It is suggested that applicants maintain consistency throughout the claims.

Claim 31 is objected to for the recitation "codes for ribosomal S12 proteins..." It is suggested that this be amended to "encodes for **the** ribosomal S12 **protein**..."

Claim 31 is objected to for the recitation "wherein the associated amino acid sequences between positions 38 to 48 in SEQ ID NO: 2..." It is suggested that this be amended to "wherein the [associated] encoded amino acids [sequences] between position[s] 38 to 48 in SEQ ID NO: 2..." Claims 32 and 33 are objected for similar reasons and it is suggested that they be amended in a similar fashion.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 24 and 31-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (claims 2-11 and 24 dependent from), 8, 31 (35 and 36 dependent from), 32 (37 dependent from), 33 (38 dependent form), 34 (39 dependent from) and 35 are indefinite in that it is vague and confusing in the recitation "which codes for ..." It is unclear what applicants intend by such a recitation. It is believed that the referred to polynucleotide sequence "encodes" for a polypeptide and for the purpose of advancing prosecution this is how the claim is interpreted. It is suggested that applicants amend the claim as such.

Claim 1 (claims 2-11 and 24 dependent from) is indefinite in that the recitation "from coryneform bacteria" is confusing and unclear. The phrase "from coryneform" is unclear as to its metes and bounds since virtually any nucleic acid can be obtained "from coryneform bacteria" acting as a host cell. Does the phrase require the claimed polynucleotide to be native to coryneform (i.e., naturally occurring in coryneform)? For

the purpose of compact prosecution, the phrase "from coryneform bacteria" is not given patentable weight as it is unclear what this phrase adds to the claim.

Claim 1 is indefinite in part c) in that the recitation "polynucleotide which is complementary" is unclear. It is unclear if it is applicants intent to claim those polynucleotides which are "fully" or "partially" complementary to the polynucleotides of a) or b). It is suggested that applicants amend the part c) of the claim to recite "polynucleotide which is fully complementary" as this is how the claim is interpreted in the interest of advancing prosecution. Claim 6 is similarly indefinite in its reference to "the sequence complementary to...".

Claims 2 is indefinite in that they recite "...a protein having the activity of the ribosomal protein S12." It is unclear what "activity of the ribosomal protein S12" applicants refer. A biologically active protein may encompass a variety of different biological activities. These include but are not limited to immunological activity, such as acting as an antigen for an antibody; regulatory activity, such as that exhibited by many proteins which control transcription and/or translation of not only their encoding nucleic acids but other nucleic acids as well; or enzymatic activity, for example, RNA polymerase activity. It is not clear what is encompassed by the "activity" of ribosomal protein S12 and if includes biological activities in addition to enzymatic activity.

Claim 2 is indefinite in that it is unclear to which "polypeptide" applicants are referring to in the recitation "wherein the polypeptide has the activity of the ribosomal protein S12. It is unclear if applicants are referring to the polypeptide of part a)

(encoded by the reference polynucleotide) or the polypeptide of part b) (encoded by the claimed polynucleotide).

Claims 6 and 7 are indefinite in the recitation of "at least one sequence which hybridizes" (claim 6) and the recitation "under a stringency corresponding to at most 2X SSC." (claim 7) as these recitations are unclear absent a statement of the **complete** conditions (i.e. salt and temperature) under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions.

Claim 6 is indefinite in that the recitation "sense mutations of neutral function in (i)" is unclear.

Claim 9 is indefinite in that it is unclear in that it is drawn to "A *Coryneform* bacterium in which the rpsL gene is enhanced." Specifically it is unclear in what an "enhanced rpsL gene" is and what it encompasses.

Claims 31-35 (36-40 dependent on) are each drawn to a DNA which originates from coryneform bacteria and has an amino acid modification at a specific residue or group of residues. It is unclear if each of these claims are drawn to DNAs comprising the "referred to reference sequence" (i.e. SEQ ID NO: 2 or SEQ ID NO: 3) with the specified modification or if each of these claims are drawn to a DNA which originates from coryneform bacteria and has an amino acid modification at a specific residue or group which corresponds to the specifically referred to reference sequence. In the second scenario, the DNA may comprise a different sequence then the reference

sequence so long as the DNA has the specified modification corresponding to the reference sequence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 7, 9, 10, 24 and 31-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 6 and 24 are directed to all possible polynucleotides which are at least 70% identical to a polynucleotide which encodes for a polypeptide of SEQ ID NO: 2, or those polynucleotides comprising a mere 15 successive nucleotides of such a polynucleotide (claims 1-4, 6, 7 and 24). Claims 7 and 9 are directed to all possible coryneform bacterium in which any rpsL gene is enhanced (claim 9) by over-expression (claim 10). Claims 31-40 are directed to all possible DNAs which originate from coryneform bacteria wherein the amino acid sequences between positions 38 to 48, or more specifically at position 43, in SEQ ID NO: 2 are modified, potentially to a specific residue, by amino acid exchange. The specification, however, only provides a single representative species of polynucleotide (i.e. SEQ ID NO: 1) encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship

in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-4, 6, 24 and 31-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any polynucleotide which comprises a mere 15 consecutive nucleotides of SEQ ID NO: 3 or is 70 identical to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4, 6 and 24 are so broad as to encompass any polynucleotide which is at a mere 70% identical to a polynucleotide which encodes a polypeptide of SEQ ID NO: 2, or those polynucleotides comprising a mere 15 successive nucleotides of such a polynucleotide. Claims 7 and 9 are so broad as to encompass any coryneform bacterium in which any rpsL gene is enhanced (claim 9) by over-expression (claim 10). Claims 31-40 are so broad as to encompass any DNA which originate from coryneform bacteria wherein the amino acid sequences between positions 38 to 48, or more specifically at position 43, in SEQ ID NO: 2 are modified, potentially to a specific residue, by amino acid exchange.

The claims rejected under this section of U.S.C. 112, first paragraph, place insufficient structural and functional limits on the claimed polynucleotides (See also above 112 second paragraph rejections). Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The same is true of a polynucleotide sequence, as the nucleic acid sequence of the polynucleotide directly correlates with the amino acid sequence of the polypeptide. However, in this case the disclosure is limited to a

polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotides sequence where nucleic acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given polynucleotide to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those polynucleotides and DNAs having the claimed structural relationship to SEQ ID NO: 1/2, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without effecting the desired activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity)

are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide with the claimed structural relationship to SEQ ID NO: 1/2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claim 11 appears to employ novel strains of *Corynebacterium, glutamicum* (i.e. strain DM1545 deposited as DSM-13992.) Since this strain is the claim, it must be obtainable by a repeatable method set forth in the specification or

otherwise be readily available to the public. These organisms are not fully disclosed, nor have they been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the specific strain of *Corynebacterium, glutamicum* (i.e. strain DM1545 deposited as DSM-13992.) Accordingly, it is deemed that a deposit of this stain should have been made in accordance with 37 CFR 1.801-1.809.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9, 10 and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Satochi et al. (EP 1 108 790, reference AP on IDS, Paper No. 4).

Satochi et al. teach a number of polynucleotides, including both DNAs and RNAs derived from coryneform bacteria. Specifically Satochi et al. teach a polynucleotide SEQ ID NO: 553 which encodes a polypeptide (SEQ ID NO: 4053 having a best local similarity score of greater then 95% to the amino acid sequence of instantly disclosed SEQ ID NO: 2. Satochi et al. further teach vectors comprising said polynucleotide and coryneform bacteria transformed with SEQ ID NO: 553. Thus claims 1-4, 6, 7, 9, 10 and 24 are anticipated by Satochi et al.

Claims 1-3, 6, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Nair et al. (Nuclèic Acids Research, Vol 21, No. 4, page 1039, 1993, reference AV on IDS, Paper No. 4).

Nair et al. teach the cloning and nucleotide sequence analysis of the ribosomal S12 gene of Mycobacterium *intracellulare*. While it is acknowledged that the taught polynucleotide is not from coryneform bacteria (see above 112 second paragraph rejection), the taught polynucleotide encodes the ribosomal S12 protein and the encoded protein has a best local similarity score of greater then 91% to the instantly disclosed polypeptide of SEQ ID NO: 2. Thus since the polynucleotide disclosed by Nair et al. meets all of the disclosed structural features of the claimed polynucleotide, claims 1-3, 6 and 7 are anticipated by Nair et al. As stated above, it is acknowledged that the polynucleotide disclosed by Nair et al. is from *Mycobacterium intracellulare* and not form a coryneform bacteria, however absent a teaching of the difference between a polynucleotide from *Mycobacterium intracellulare* versus a polynucleotide from a coryneform bacteria, the polynucleotide taught by Nair et al. is considered to anticipate the claimed polynucleotide, regardless of its origin.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh